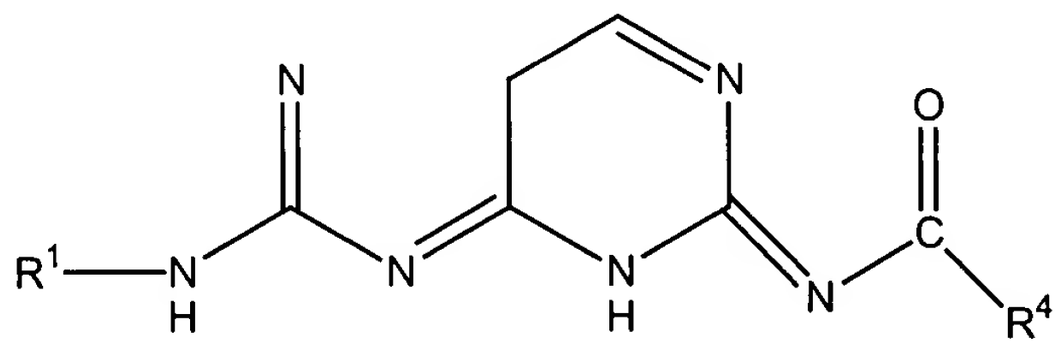
Please add, after the chemical structure and immediately below it:

A1

--



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On page 37, after the last two chemical structures, and directly below said structures, please add

A2

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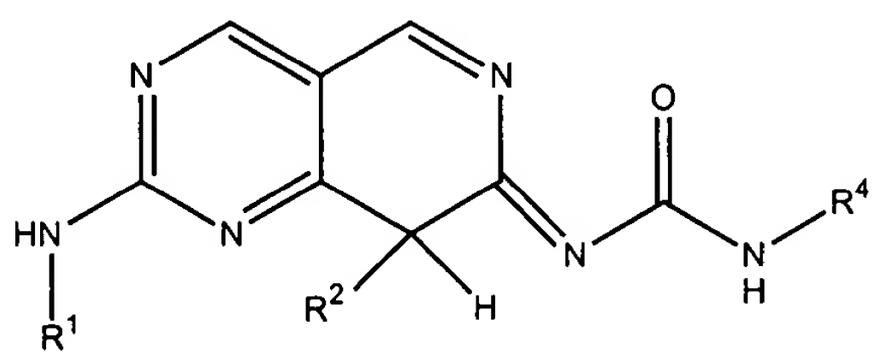
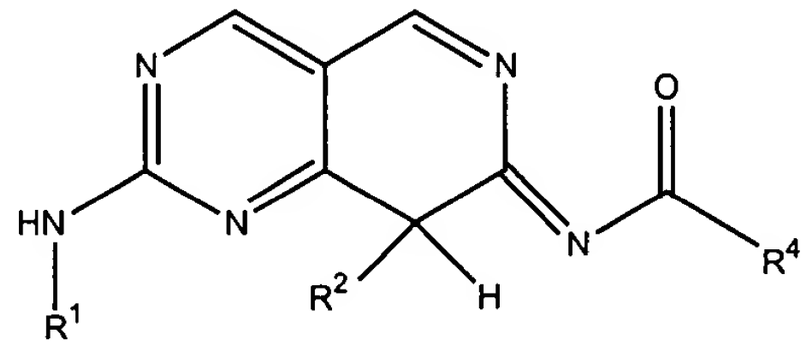


or



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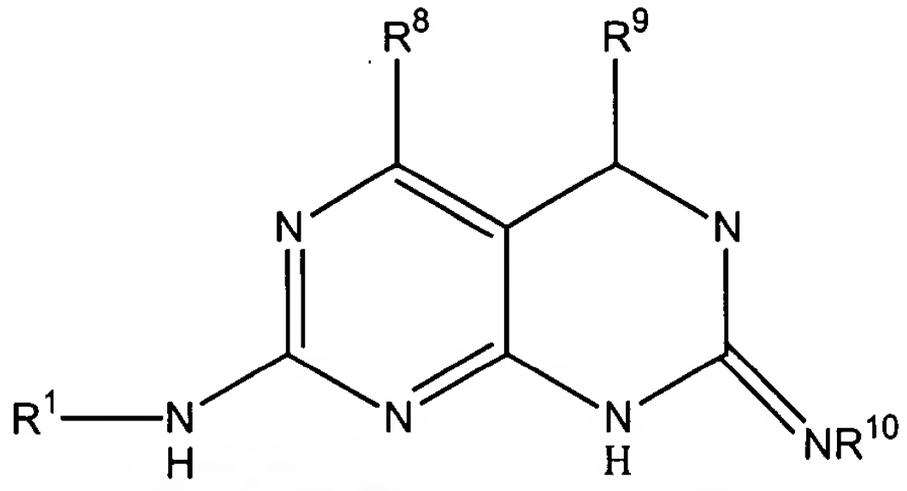
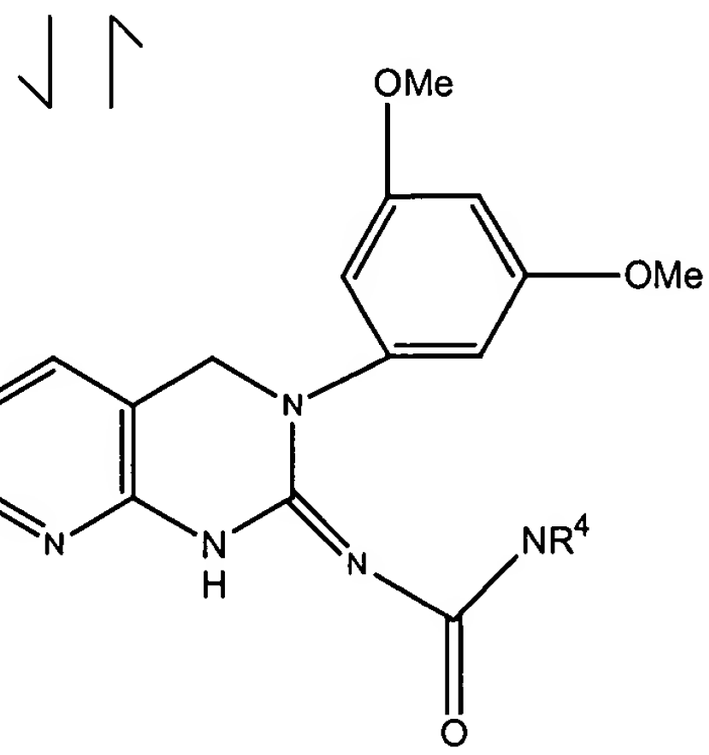
On page 40, after the chemical structure at line 11, and directly below it, please insert

A3

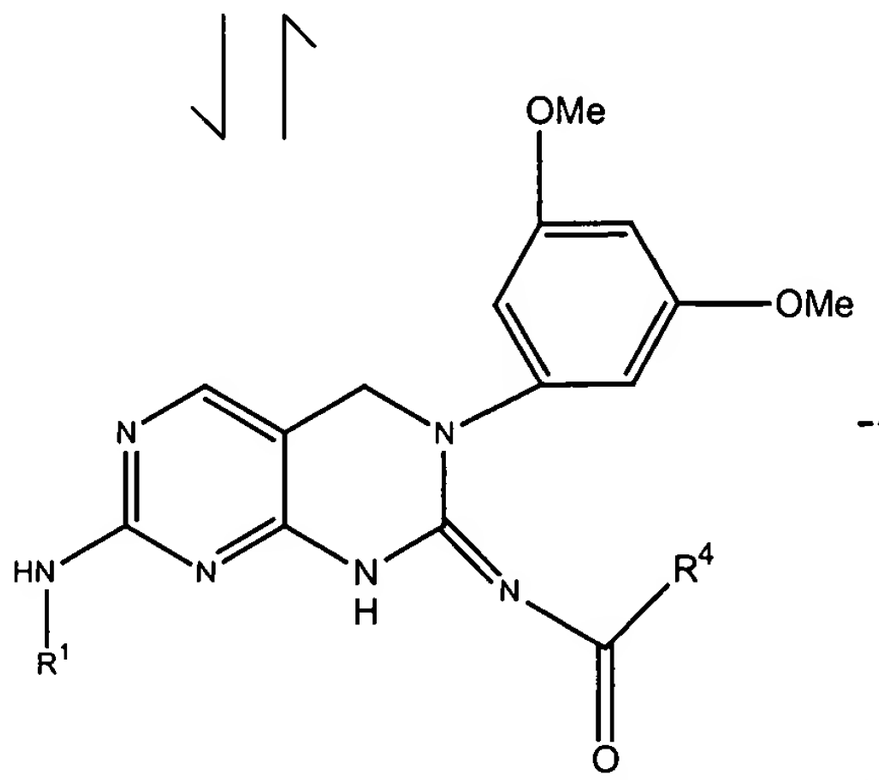
--  --

On page 41, after the last two chemical structures, and directly below them, please insert:

A4

-- 

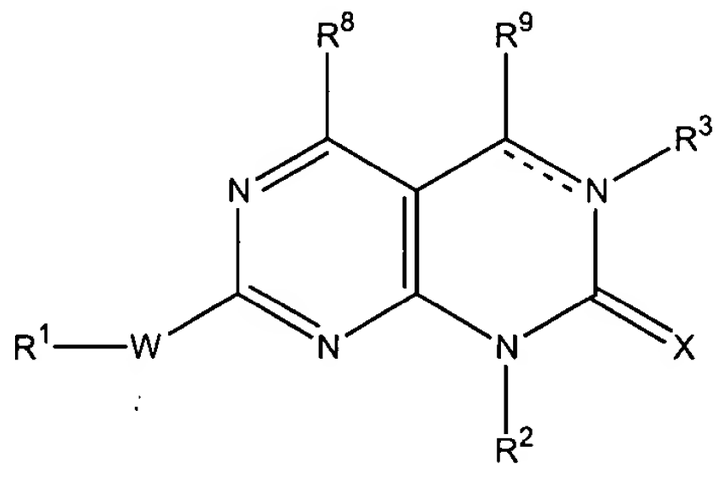
or

 --

Please add, as page 132, the Abstract enclosed herewith on a separate sheet.

IN THE CLAIMS:

Claim 1 (amended). A compound of Formula I



I

and the pharmaceutically acceptable salts thereof,

wherein:

the dotted line represents an optional double bond;

W is NH, S, SO, or SO_2;

X is either O, S, or NR^{10};

R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,

$$\begin{array}{c} OR^5 \\ | \\ \text{heteroaryloxy, } T(CH_2)_mQR^4, T(CH_2)_mC\text{-}(CH_2)_mQR^4, \\ | \\ H \end{array}$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, or $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4,

$N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$, or $N^+R^5R^6Y^-$;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as

OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;

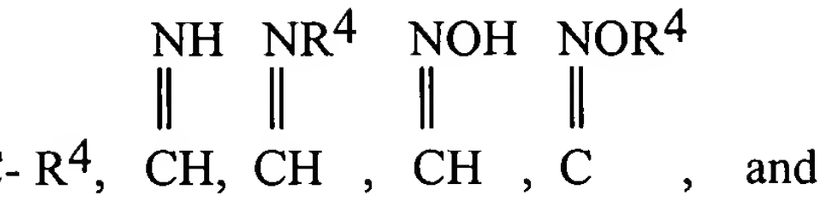
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1\text{-}C_6\text{alkyl})_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$.

R^6 is alkyl;

R^8 and R^9 independently are H, C_1-C_3 alkyl, NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CHO, CN, or NO_2;

when the dotted line is absent, R^9 is additionally oxo,



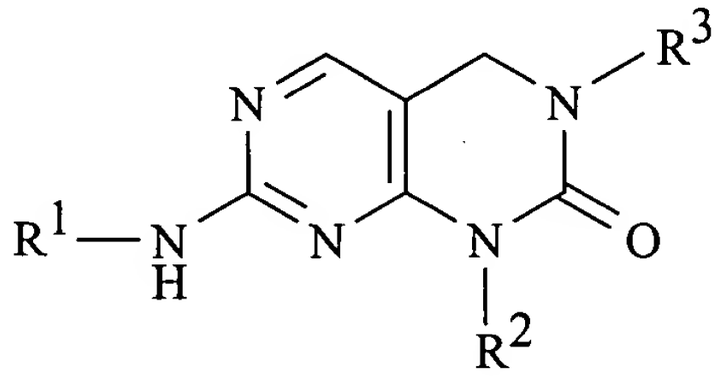
AS Cont

Y is a halo counter-ion.

Claim 2 (amended). A compound of Claim 1 wherein W is NH, and R^8, and R^9 both are hydrogen.

Claim 7 (amended). A compound of Claim 2 having the formula

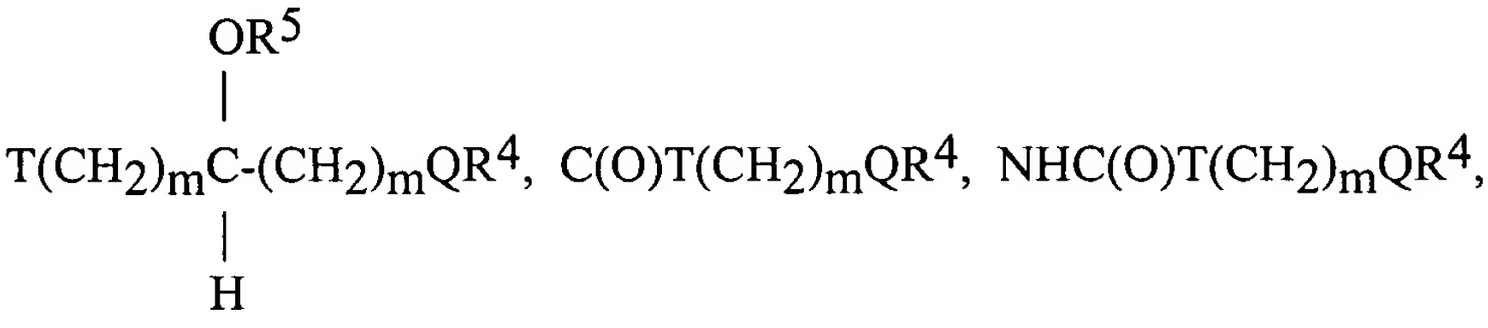
A6



wherein:

R^1, R^2 and R^3 independently are hydrogen, C_1-C_{10} alkyl, $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, C_3-C_{10} cycloalkyl, $(CH_2)_n$ C_3-C_{10} cycloalkyl, or $(CH_2)_n$heteroaryl,

wherein n is 0, 1, 2 or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl and heterocyclyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro, heteroaryloxy, $T(CH_2)_mQR^4$,



$T(CH_2)_mC(O)NR^4NR^5$, or $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$, or $N^+R^5R^6Y^-$;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

A6 Cont

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1\text{-}C_6\text{alkyl})_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, C_1-C_3 alkyl, NR^4R^5, $N^+(O)R^4R^5$,

$N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4,

$CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CHO, CN, or NO_2;

A6 Cont

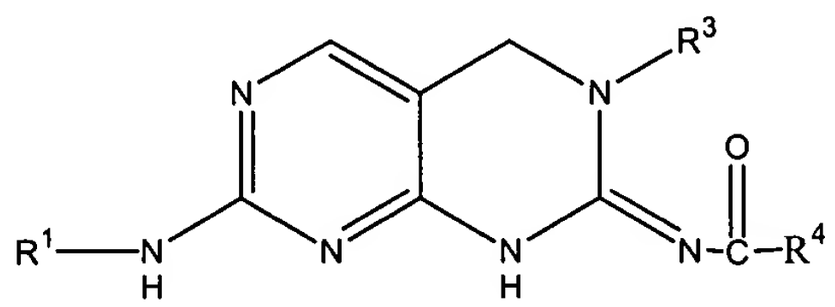
when the dotted line is absent, R^9 is additionally oxo,

S	NH	NR^4	NOH	NOR^4	
C- R^4,	CH,	CN,	CH,	C,	and

Y is a halo counter-ion.

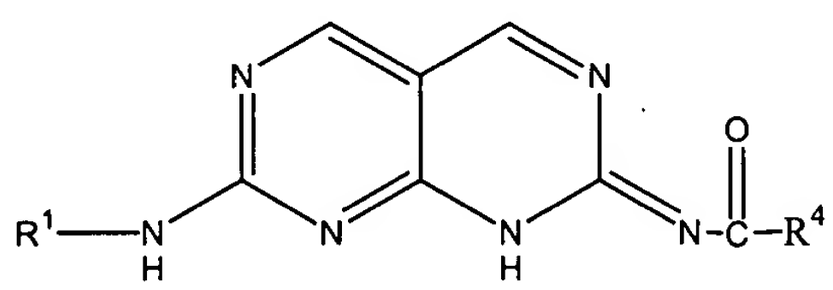
Claim 10 (amended). A compound of Claim 2 having the formula

A7



Claim 12 (amended). A compound of Claim 2 having the formula

A8



Claim 17 (cancelled).

Claim 18 (cancelled).

Claim 19 (cancelled).

Claim 20 (cancelled).

Claim 21 (cancelled).

Claim 22 (cancelled).

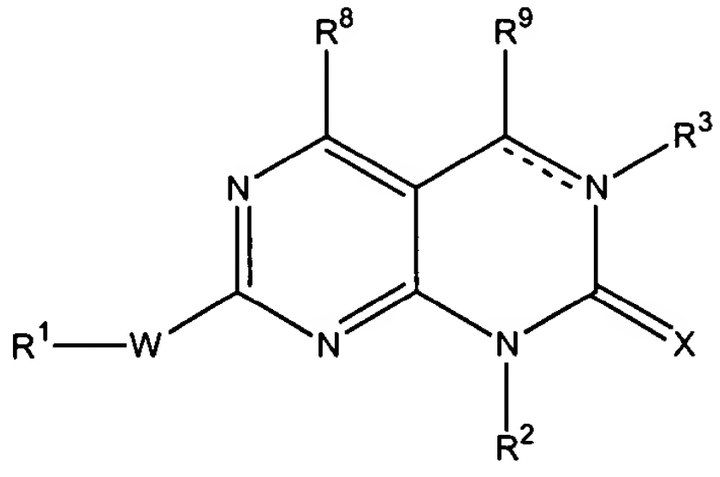
Claim 23 (cancelled).

Claim 24 (cancelled).

Claim 25 (cancelled).

Claim 26 (amended). A method of inhibiting a cyclin-dependent kinase comprising contacting the cyclin-dependent kinase with a compound of Formula I

A9



I

and the pharmaceutically acceptable salts thereof,

wherein:

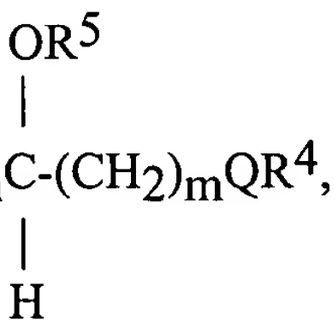
the dotted line represents an optional double bond;

W is NH, S, SO, or SO_2;

X is either O, S, or NR^{10};

R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected

from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,



heteroaryloxy, $T(CH_2)_mQR^4$, $T(CH_2)_mC(OR^5)H-(CH_2)_mQR^4$,

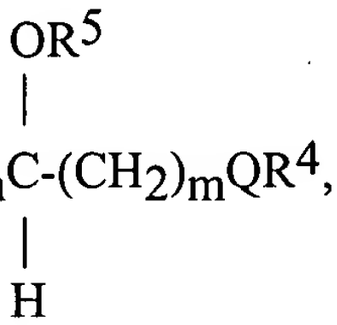
AG Cont

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, or $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$, or $N^+R^5R^6Y^-$;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as

OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,



$T(CH_2)_mQR^4$, $T(CH_2)_mC(OR^5)H-(CH_2)_mQR^4$,

wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1$-C_6alkyl$)_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from

OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, T-$(CH_2)_mQR_4$,

CO-T-$(CH_2)_mQR^4$, NH(CO)T$(CH_2)_mQR^4$, T-$(CH_2)_mCO_2R^4$, or

T$(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

A9 Cont

R^8 and R^9 independently are H, C_1-C_3 alkyl, NR^4R^5, $N^+(O)R^4R^5$,

$N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4,

$CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CHO, CN, or NO_2;

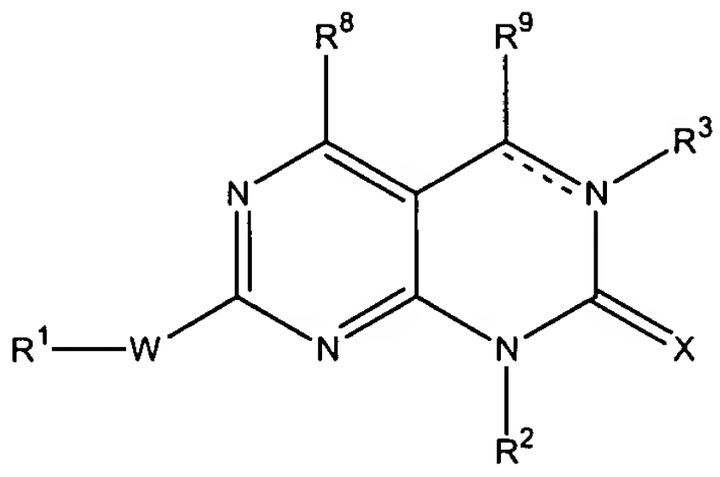
when the dotted line is absent, R^9 is additionally oxo,

S NH NR^4 NOH NOR^4
‖ ‖ ‖ ‖ ‖
C- R^4, CH, CH , CH , C , and

Y is a halo counter-ion.

Claim 30 (amended). A method of inhibiting a growth factor-mediated tyrosine kinase comprising contacting said growth factor-mediated kinase with a compound of Formula I

A10 Cont



I

and the pharmaceutically acceptable salts thereof,

wherein:

the dotted line represents an optional double bond;

W is NH, S, SO, or SO_2;

X is either O, S, or NR^{10};

R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,

A10 Cont

$$\text{heteroaryloxy, } T(CH_2)_mQR^4, T(CH_2)_mC(OR^5)\text{-}(CH_2)_mQR^4, T(CH_2)_mC(H)\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, or $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$, or $N^+R^5R^6Y^-$;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

$$T(CH_2)_mQR^4, T(CH_2)_mC(OR^5)\text{-}(CH_2)_mQR^4, T(CH_2)_mC(H)\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1\text{-}C_6\text{alkyl})_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and

heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$;

A10 cont

R^6 is alkyl;

R^8 and R^9 independently are H, C_1-C_3 alkyl, NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CHO, CN, or NO_2;

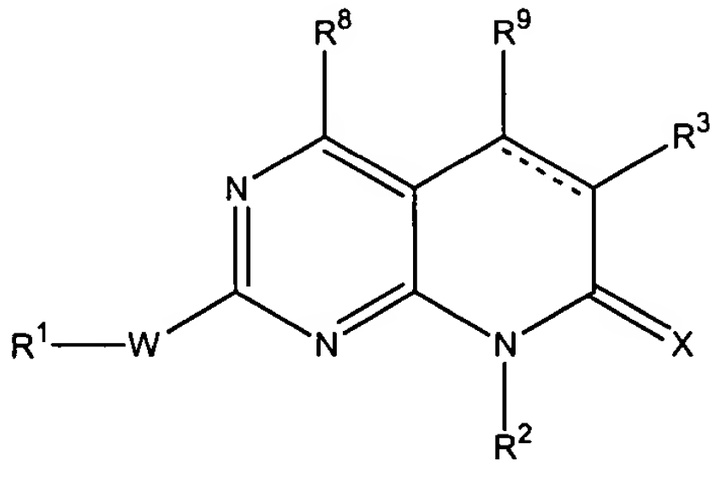
when the dotted line is absent, R^9 is additionally oxo,

S NH NR^4 NOH NOR^4
‖ ‖ ‖ ‖ ‖
C- R^4, CH, CH , CH , C , and

Y is a halo counter-ion.

Claim 34 (amended). A method of inhibiting a non-receptor tyrosine kinase comprising contacting said non-receptor tyrosine kinase with a compound of Formula I

A11



I

and the pharmaceutically acceptable salts thereof,

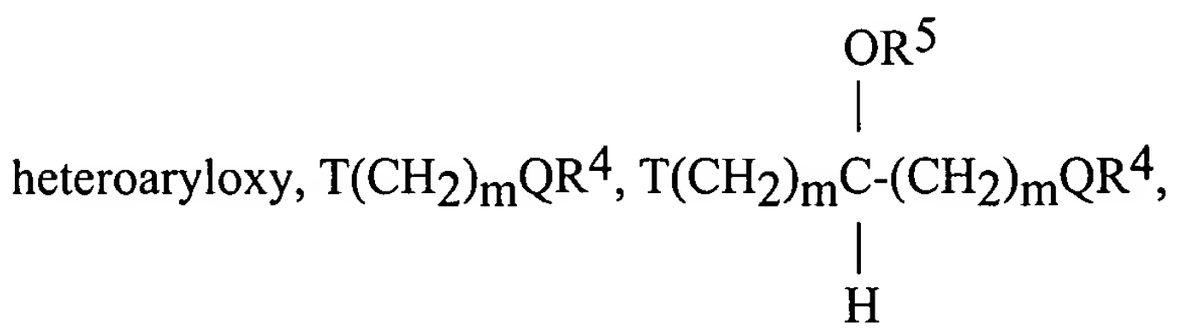
wherein:

the dotted line represents an optional double bond;

W is NH, S, SO, or SO_2;

X is either O, S, or NR^{10};

R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,



heteroaryloxy, $T(CH_2)_mQR^4$, $T(CH_2)_mC(OR^5)H$-$(CH_2)_mQR^4$,

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, or $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N(O)R^5$, or NR^5R^6Y;

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1\text{-}C_6alkyl)_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

A11 Cont

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, or $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, C_1-C_3 alkyl, NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, hydroxy, alkoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CHO, CN, or NO_2;

when the dotted line is absent, R^9 is additionally oxo,

$$S\text{-}R^4,\ NH,\ NR^4,\ NOH,\ NOR^4$$

and

Y is a halo counter-ion.

Claim 37 (amended). A method of treating a subject suffering from vascular smooth muscle cell proliferation comprising administering to said subject a therapeutically effective amount of a compound of Claim 1.

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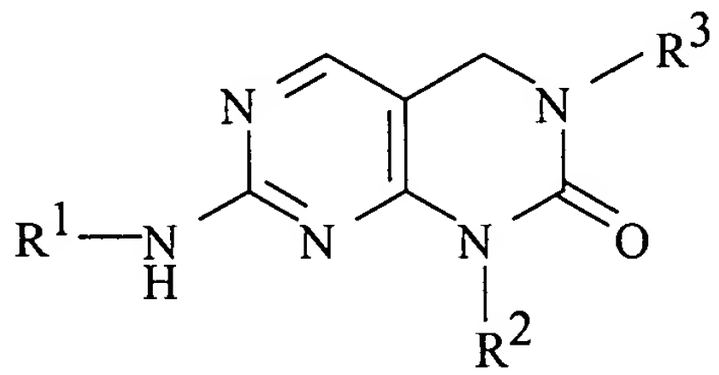
Claim 38 (cancelled).

Claim 40 (cancelled).

Please add new Claims 44-53:

Claim 44 (new). A compound of the formula

A13



wherein:

R^1 is C_1-C_{10} alkyl or $(CH_2)_nAr$;

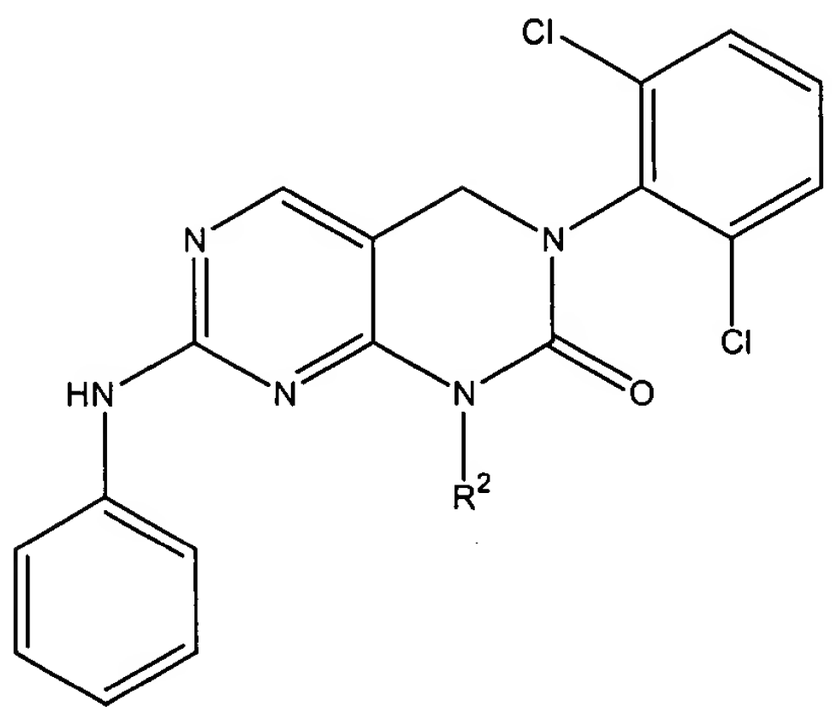
R^2 is H, C_1-C_{10} alkyl, or $(CH_2)_nAr$; and

R^3 is Ar,

wherein n is 0, 1, 2 or 3;

Ar is phenyl or phenyl substituted with one or two groups selected from halo, alkyl, or substituted alkyl; or a pharmaceutically acceptable salt thereof.

Claim 45 (new). A compound of the formula



A13 Cont

wherein R^2 is $(CH_2)_nAr$, n is 0, 1, 2 or 3, and Ar is phenyl or phenyl substituted by a 2-aminoethyl group,
or a pharmaceutically acceptable salt thereof.

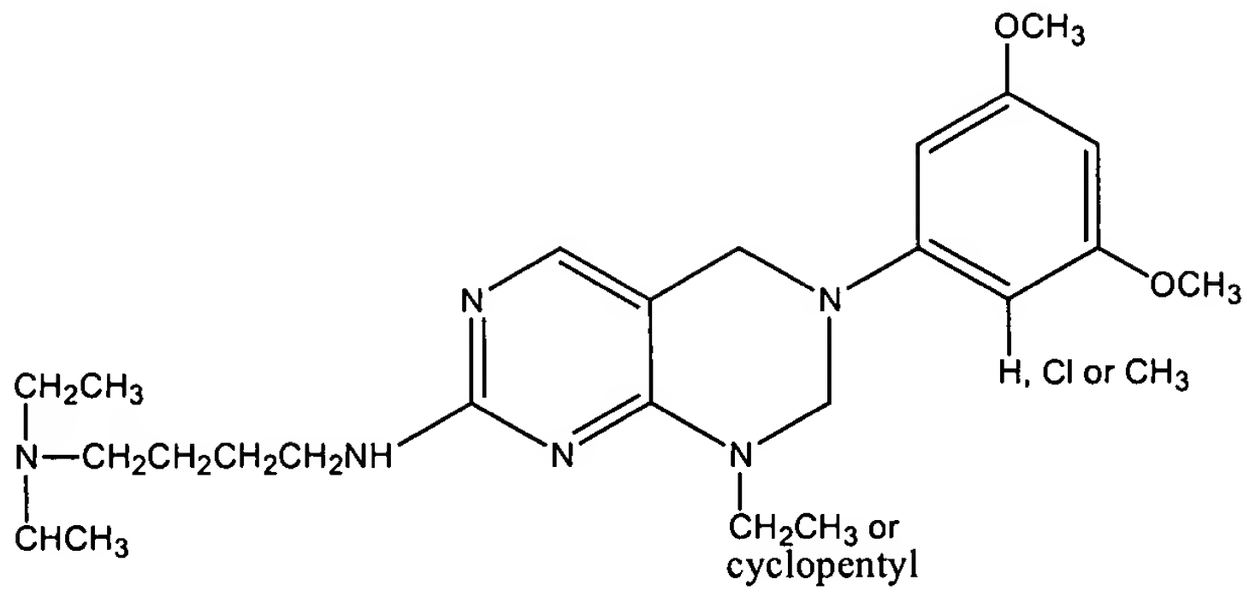
Claim 46 (new). A pharmaceutical formulation comprising a compound of Claim 3 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 47 (new). A pharmaceutical formulation comprising a compound of Claim 7 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 48 (new). A pharmaceutical formulation comprising a compound of Claim 44 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 49 (new). A pharmaceutical formulation comprising a compound of Claim 45 in combination with a pharmaceutically acceptable carrier, diluent or excipient.

Claim 50 (new). A compound of the formula



A13 Cont

or a pharmaceutically acceptable salt thereof.

Claim 51 (new). The compound 7-(4-diethylamino-butylamino)-3-(2-chloro-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidine-2(1*H*)-one.

Claim 52 (new). The compound 7-(4-diethylamino-butylamino)-3-(2-methyl-3,5-dimethoxy-phenyl)-1-ethyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidine-2(1*H*)-one.

Claim 53 (new). The compound 7-(4-diethylamino-butylamino)-3-(3,5-dimethoxy-phenyl)-1-cyclopentyl-3,4-dihydro-pyrimido[4,5-*d*]pyrimidine-2(1*H*)-one.